alpha-glucosylmyricitrin, alpha-glucosylisoquercitrinin, alpha-glucosylquercitrin, myricetin, rhamnetin, apigenin, naringin, hesperidin, hesperitin, morin, phloridzin, diosmin, vitexin, neohesperidin dihydrochalcone, flavone, glucosylrutin and genistein;

D2 Cont

b) optionally one or more cinnamic acid derivatives; and

c) optionally an antioxidant. --

--33. The cosmetic or dermatological formulation according to claim 32, which comprises an antioxidant. --

REMARKS

In this continued prosecution application, Applicants intend to continue the prosecution from the point at which prosecution was terminated in the parent application.

Before addressing the substantive issues, Applicants point out that the previous claims have been replaced by a new set of claims. For the Examiner's convenience, Applicants point out that the new claims correspond to the previous claims as follows:

New Claim	Previous Claim
19	8 (But claim 19 is limited to preventing or treating immunosuppression)
20, 21	11
22	12
23	New (Claim 23 is a combination of claims 8 + 12)
24	13
25	8 (But claim 25 is limited to protecting cells which participate in the immune response of the skin)
26, 27	11
28	12
29	New (Claim 29 is a combination of claims 8 + 12)
30, 31	14
32, 33	14

No new matter is added by this amendment.

At the time that prosecution was terminated in the parent application, claims 8, 13-16 and 18 were rejected under 35 USC § 102(b) as being anticipated by Suzuki et al.("Suzuki"), U.S. Patent No. 5,145,781. In response, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

1. The Formulation Claims

Regarding the formulation claims, the Examiner says that the recitation of "optionally" does not limit the instant formulations to further contain the optional components. In response, Applicants point out that new claim 30 requires the presence of both the flavonoids and the cinnamic acid derivatives. New claim 31 requires the presence of the flavonoids, the cinnamic acid derivatives and an antioxidant. Consequently, Applicants do not believe that these claims are anticipated by Suzuki.

Formulation claims 32 and 33 still recite "optionally," but the list of flavonoids in clause "a" does not include alpha-glucosylrutin. Accordingly, Applicants also do not believe that these claims are anticipated by Suzuki.

2. The Method Claims

With respect to the method claims, Applicants point out that claims 20-23 and 26-29 all require the presence of both the flavonoids and the cinnamic acid derivatives. Consequently, Applicants do not believe that these claims are anticipated by Suzuki.

Method claims 19, 24, 25 still recite "optionally," and, therefore, cover the use of alpha-

glucosylrutin alone. However, Applicants submit that these methods also are not anticipated by Suzuki.

In this regard, Applicants would remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, if the Examiner relies on a theory of inherency as to any particular element, then the extrinsic evidence must make clear that such element is *necessarily* present in the thing described in the reference, and the presence of such element therein would be so recognized by persons skilled in the art. *In re Robertson,* 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Further, inherency is not established by probabilities or possibilities, and the mere fact that a property may result from a given circumstances is not sufficient; instead it must be shown that such property *necessarily* inheres in the thing described in the reference. *Id.*

The Examiner finds that Suzuki discloses the use of α-glucosyl rutin "as preventive remedy, UV absorbent, and promoter for healing injury and burn." However, the Examiner has not shown such uses to be identical with the purpose of the present claims. Thus, new claims 19 and 24, as did previous claims 8, 11-13, 15, 16 and 18, require that the α-glucosyl rutin be topically applied to the skin of a patient for the specific purpose of preventing or treating immunosuppression of skin cells induced by UVB radiation. The use required by the present

claims appears to be different from that found to be taught by Suzuki, and the Examiner has not explained anywhere how the present use is identical to Suzuki's uses or why persons skilled in the art would have recognized that the present use is inherent in Suzuki's uses. In the absence of such explanation, Applicants submit that the Examiner has not made out a *prima facie* case of anticipation.

Further on this point, the Examiner says that skin injury and burn are clinical conditions manifested by signs of inflammation. Nevertheless, it does not follow that all skin injuries, burns, and inflammation must be due to immunosuppression of skin cells induced by UVB radiation. Unless this is the case, it cannot be said that Suzuki's promotion of healing injury and burn *necessarily* involves prevention or treatment of immunosuppression of skin cells induced by UVB, as required by the instant claims.

In a similar manner, new claim 25, as did previous claims 8, 11-13, 15, 16 and 18, requires that the α-glucosyl rutin be topically applied to the skin of a patient for the specific purpose of protecting the cells which participate in the immune response of the skin from the damaging effects of UVB radiation. Again, the use required by claim 25 appears to be different from that found to be taught by Suzuki, and the Examiner has not explained anywhere how the present use is identical to Suzuki's uses or why persons skilled in the art would have recognized that the present use is inherent in Suzuki's uses. In the absence of such explanation, Applicants

submit that the Examiner has not made out a *prima facie* case of anticipation.

In view of the foregoing, Applicants respectfully submit that the Examiner would be fully justified to reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Claims 8,11-16 and18 were rejected under 35 USC § 103(a) as being obvious over Nakamura et al. ("Nakamura"), U.S. Patent No. 5,561,116 in view of Whittle, U.S. Patent No. 5,466,452, and Nakanishi et al. ("Nakanishi"), U.S. Patent No. 5,008,441. In response, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well.

According to *Manual of Patent Examining Procedure* ("MPEP") § 2143:

> "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combincd) must teach or suggest all the claim limitations."

Applicants respectfully submit that none of these criteria have been satisfied in the instant case. First, there is no teaching or suggestion or any other evidence of motivation in the cited combination of references to apply flavonoids topically to the skin in order to prevent or treat immunosuppression of skin cells induced by UVB radiation or to protect the cells which participate in the immune response of the skin from the damaging effects of UVB radiation. As will be explained in greater detail below, the prior art fails to teach the specific purpose presently claimed, and, also, does not even teach the exact role of flavonoids in the prior art purpose. Second, in view of the foregoing, the prior art does not reveal a reasonable expectation that topical application of flavonoids to skin would be successful to prevent or treat immunosuppression of skin cells induced by UVB radiation or to protect the cells which participate in the immune response of the skin from the damaging effects of UVB radiation. Third, as indicated, the prior art nowhere teaches the claimed result of preventing or treating immunosuppression of skin cells induced by UVB radiation or of protecting the cells which participate in the immune response of the skin from the damaging effects of UVB radiation, and, therefore, not all limitations of the present claims are taught or suggested by the cited combination of references.

1. The Formulation Claims

With respect to the formulation claims, Applicants submit that the cited combination of

references does not lead persons skilled in the art to the combinations now claimed. Formulation claims 30 and 31 require the presence of one or more particular hydroxycinnamic acid derivatives of the formula recited, and these are not shown in any of the cited references, nor have they been shown to be obvious therefrom. Consequently, Applicants submit that these claims are not *prima facie* obvious from the cited combination of references.

Formulation claims 32 and 33 recite "optionally," and, therefore, do not require the presence of the one or more hydroxycinnamic acid derivatives in the formulations covered thereby. Nevertheless, Applicants submit that the subject matter of claims 32 and 33 also is not rendered *prima facie* obvious from the cited combination of references.

The Examiner relies on Nakamura to show Propolis extracts, and alleged they contain many different compounds, including flavonoids (e.g. chrysin, Kaempferol, quercetin) and cinnamic acid derivatives, such as ferulic acid. Nakamura refers to Propolis being known for stimulating and regeneration of tissue (col. 2, line 11), and at col. 8, lines 32-34 teaches that it can be incorporated into an ointment. At col. 2, lines 64-66, Nakamura mentions that Propolis has anti-inflammatory, burn-healing and wound-healing properties. This however, does not necessarily mean that Propolis is useful for treatment or prophylaxis of immunosuppression of the skin cells induced by UVB radiation. Burns, wounds and inflammation can result for reasons having nothing to do with UVB. Even if someone might have used Propolis for treating e.g. a

burn sustained from contacting something hot, one would not know to treat sunburn with Propolis.

In addition it is the extract of Propolis that is used for the various treatments disclosed, and the reference does not seem to show that any of the specific flavonoids Applicants have claimed actually end up in the extract. See col. 3, lines 16-17. Thus, attached is page 39347 of the Römpp-Chemie-Lexikon. This page conforms that rutin, a flavonoid, and similar in structure to alpha-glucosylrutin, which has an additional glucose substituent is not soluble in Chloroform, Ether, CS_2, Benzol, Petrolether (all organic solvents and not miscible with water) but soluble in Pyridine, Dimethylformamide, Ethanol Acetone (all organic solvents and miscible with water). It may be that flavonoids are not soluble in "nonpolar" organic solvents which are not miscible with water. Since the solubility of flavonoids in organic solvents is not certain, there can be no reasonable expectation that Nakamura's extracts actually contain flavonoids, or that, therefore, flavonoids make up part of the composition applied to the skin during the course of the disclosed treatment.

2. *The Method Claims*

With respect to the method claims, Applicants submit that the cited combination of references does not teach or suggest that topical application of flavonoids is effective to prevent

or treat immunosuppression of skin cells induced by UVB radiation or to protect the cells which participate in the immune response of the skin from the damaging effects of UVB radiation. The Examiner says the limitations of the claims are met because the prior art teaches effective treatment of an inflammatory response when a "flavonoid *containing* topical product" is applied to skin. However, this is *not* what is claimed. What is claimed, or, more accurately, what is required by the claims, is that *the* flavonoid is *the* effective agent responsible for the claimed result. Reading the cited combination of refcrences, one is left without any clue as to the role of the flavonoid in the prior art compositions, *if they are actually present therein,* or the results achieved thereby. Accordingly, there is no teaching or suggestion anywhere in the cited combination of references that flavonoids can be administered to prevent or treat immunosuppression of skin cells induced by UVB radiation or to protect the cells which participate in the immune response of the skin from the damaging effects of UVB radiation. Not only does the cited combination of references fail to teach the result required by the instant claims, but they also fail to teach or suggest any role of flavonoids in accomplishing that result. Accordingly, it cannot be said that given the cited combination of references it would have been obvious at the time the present invention was made to apply flavonoids topically to skin in order to prevent or treat immunosuppression of skin cells induced by UVB radiation or to protect the cells which participate in the immune response of the skin from the damaging effects of UVB radiation. Consequently, the method claims cannot be obvious from the cited combination of references.

The Examiner also finds that because the prior art teaches effective treatment of an inflammatory response by applying a flavonoid containing topical product to skin, therefore, the source inducing an inflammatory response does not impart patentability to the claims. Applicants submit that there is absolutely no support for such a position in the patent law, and it amounts to a failure to consider all claim limitations, which, as should be clear from the quote above, is a clear error. Unless the Examiner can show – which he has not – that all inflammatory responses have a common source and a common treatment, which common sense alone suggests is not correct, it cannot be said that the source of the inflammation is unimportant. Here, the prior art not only fails to teach the specific purpose required by the instant claims, but it also fails to teach the role of flavonoids in the claimed purpose or even in the inflammatory response relied on so heavily by the Examiner. Again, it cannot be said that it would have been obvious given the cited combination of references to apply flavonoids topically to the skin in order to prevent or treat immunosuppression of skin cells induced by UVB radiation or to protect the cells which participate in the immune response of the skin from the damaging effects of UVB radiation.

In view of the foregoing, Applicants respectfully submit that the Examiner would be fully justified to reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Early and favorable action is earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the foregoing Preliminary Amendment and the accompanying Request for a Continued Prosecution Application, Petition for Extension of Time, and Information Disclosure Statement + Form 1449 + 1 Reference (34 pages total) are being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below:

Date: January 31, 2002

By _____
William C. Gerstenzang